WHAT IS CLAIMED AS BEING NOVEL & UNOBVIOUS IN UNITED STATES LETTERS PATENT IS:

1. A pharmaceutical composition, comprising

a surfactant; and

a nucleic acid which comprises an oligonucleotide (oligo) effective to alleviate bronchoconstriction, allegy (ies) or inflammation, the oligo being selected from the group consisting of oligonucleotides which are

anti-sense to target genes and mRNAs corresponding to the target genes, to genomic flanking regions selected from the group consisting of intron and exon borders selected from the group consisting of the 5' end, the 3' end and the juxta-section between coding and non-coding regions, and to all segments of mRNA(s) encoding an adenosine A_1, A_{2b} and A_3 receptors;

anti-sense to target genes and mRNAs corresponding to the target genes, to genomic flanking regions selected from the group consisting of intron and exon borders selected from the group consisting of the 5' end, the 3' end and the juxta-section between coding and non-coding regions, and to all segments of mRNA(s) encoding an adenosine A_1, A_{2b} and A_3 receptors, and consist of less than about 15% adenosine (A);

combinations of the oligos;

pharmaceutically acceptable salts of the oligos; and

mixtures of the oligos, their combinations and their salts.

2. The composition of claim 1, wherein the oligo consists of up to about 10% A.

3. The composition of claim 2, wherein the oligo consists of up to about 5% A.

4. The composition of claim 3, wherein the oligo consists of up to about 3% A.

5. The composition of claim 4, wherein the oligo is A-free.

6. The composition of claim 1, wherein the target gene is selected from

the group consisting of genomic flanking regions, target genes, , sequences comprising an initiation codon, sequences comprising 2 or more G and/or C nucleotides, mRNAs and bridging sections thereof of the adenosine A1 receptor.

7. The composition of claim 1, wherein the target gene is selected from the group consisting of genomic flanking regions, target genes, , sequences comprising an initiation codon, sequences comprising 2 or more G and/or C nucleotides, mRNAs and bridging sections thereof of the adenosine A_{2a}, A_{2b} and A_3 receptor.

8. The composition of claim 1, wherein one A is substituted by a universal base selected from the group consisting of heteroaromatic bases which bind to a thymidine base but have antagonist activity and less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, and heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

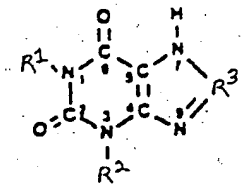
9. The composition of claim 8, wherein all As are substituted by universal bases selected from the group consisting of heteroaromatic bases which bind to a thymidine base but have antagonist activity and less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, and heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

10. The composition of claim 8, wherein the heteroaromatic bases are selected from the group consisting of pyrimidines and purines, which may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH and branched and fused primary and secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, which may be further substituted by O, halo, NH_2,

primary, secondary and tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl and heteroaryl.

11. The composition of claim 10, wherein the pyrimidines and purines are substituted at a position selected from the group consisting of positions 1, 2, 3, 4, 7 and 8.

12. The composition of claim 11, wherein the pyrimidines and purines are selected from the group consisting of theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline and xantine having the chemical formula



wherein R^1 and R^2 are independently H, alkyl, alkenyl or alkynyl and R^3 is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH_2-alkylamino-ketoxyalkyloxy-aryl and mono and dialkylaminoalkyl-N-alkylamino-SO_2 aryl.

13. The composition of claim 12, wherein the universal base is selected from the group consisting of 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methoxyaminopurine.

14. The composition of claim 1, where a methylated cytosine (^mC) is substituted for a C in at least one CpG dinucleotide if present in the oligo(s).

15. The composition of claim 1, wherein at least one mononucleotide linking phosphodiester residue of the anti-sense oligonucleotide(s) is selected from the group consisting of methylphosphonate, phosphotriester, phosphorothioate,

phosphorodithioate, phosphorotrithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methylimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues and combinations thereof.

16. The composition of claim 15, wherein all phosphodiester residues are selected from the group consisting of methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, phosphorotrithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methylimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues and combinations thereof.

17. The composition of claim 1, wherein the anti-sense oligonucleotide comprises about 7 to 60 mononucleotides.

18. The composition of claim 1, wherein the anti-sense oligonucleotide comprises SEQ ID NOS: 1, 3, 5, 7 and fragments 1-957 (SEQ. ID NO: 8-957) of SEQ. ID NO:7, and SEQ. ID NOS: 953-996.

19. The composition of claim 1, wherein the anti-sense oligonucleotide is linked to an agent selected from the group consisting of cell internalized or up-taken agent(s) and cell targeting agents.

20. The composition of claim 19, wherein the cell internalized or up taken agent is selected from the group consisting of transferrin, asialoglycoprotein and streptavidin.

21. The composition of claim 19, wherein the nucleic acid is linked to a vector.

22. The composition of claim 21, wherein the vector is selected from the group consisting of prokaryotic and eukaryotic vectors.

23. The composition of claim 1, wherein the surfactant is selected from the

group consisting of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D and surfactant protein and active fragments thereof, non-dipalmitoyl disaturated phosphatidylcholine, dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholin, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycero-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate, artificial lamellar bodies vehicles for surfactant components, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitic acid, non-ionic ethylene and/or propylene oxide block copolymers, polyoxypropylene, polyoxyethylene, poly (vinyl amine) with dextran and/or alkanoyl side chains, Brij 35, Triton X-100, ALEC, Exosurf, Survant and Atovaquone.

24. A cell, comprising the nucleic acid of claim 1.

25. The composition of claim 1, further comprising a carrier.

26. The composition of claim 25, wherein the carrier comprises a biologically acceptable carrier.

27. The composition of claim 26, wherein the carrier comprises a pharmaceutically or veterinarily acceptable carrier.

28. The composition of claim 25, wherein the carrier is selected from the group consisting of gaseous, liquid, solid carriers and mixtures thereof.

29. The composition of claim 25, further comprising an agent selected from the group consisting of other therapeutic agents, antioxidants, flavoring and coloring agents, fillers, volatile oils, buffering agents, dispersants, RNA inactivating agents, flavoring agents, propellants and preservatives.

30. The composition of claim 29, comprising the nucleic acid, the

surfactant, a therapeutic agent and a pharmaceutically acceptable carrier.

31. The composition of claim 30, wherein the therapeutic agent is selected from the group consisting of other anti-adenosine A_1, A_{2b} and A_3 receptor agents, other anti-arrhythmic agents, anti-inflammatory agents, anti-bacterial agents, anti-sepsis agents, adenosine and agents exhibiting adenosine agonist activity, analgesics, diuretics, kidney activity maintenance and restoration agents and agents for the treatment of pulmonary vasoconstriction, inflammation, allergies, asthma, Acute Respiratory Distress Syndrome (ARDS), ischemia, impeded and blocked respiration, respiratory distress syndrome, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD), and cancers selected from the group consisting of leukemias, lymphomas and carcinomas of the colon, breast, lung, pancreas, hepatocellular carcinoma, kidney, melanoma, hepatic, lung, breast and prostate metastatic cancer, radiation agents, chemotherapeutic agents, antibody therapy agents and phototherapeutic agents.

32. The composition of claim 29, wherein the RNA inactivating agent comprises an enzyme.

33. The composition of claim 32, wherein the enzyme comprises a ribozyme.

34. The composition of claim 1, wherein the anti-sense oligonucleotide is present in an amount of about 0.01 to about 99.99 w/w of the composition.

35. The composition of claim 34, wherein the anti-sense oligonucleotide is present in an amount of about 1 to about 40 w/w of the composition.

36. A formulation, comprising the composition of claim 25, selected from the group consisting of systemic and topical formulations.

37. The formulation of claim 36, selected from the group consisting of oral, intrabuccal, intrapulmonary, rectal, intrauterine, intratumor, intracranial, nasal, intramuscular, subcutaneous, intravascular, intrathecal, inhalable, transdermal,

intradermal, intracavitary, implantable, iontophoretic, ocular, vaginal, intraarticular, otical, intravenous, intramuscular, intraglandular, intraorgan, intralymphatic, implantable, slow release and enteric coating formulations.

38. The formulation of claim 37, which is an oral formulation, wherein the carrier is selected from the group consisting of solid and liquid carriers.

39. The formulation of claim 38, wherein the liquid carrier is selected from the group consisting of solutions, suspensions, and oil-in-water and water-in-oil emulsions.

40. The formulation of claim 38, which is selected from the group consisting of a powder, dragees, tablets, capsules, sprays, aerosols, solutions, suspensions and emulsions.

41. The formulation of claim 36, which is a topical formulation, wherein the carrier is selected from the group consisting of creams, gels, ointments, sprays, aerosols, patches, solutions, suspensions and emulsions.

42. The formulation of claim 36, which is an injectable formulation, wherein the carrier is selected from the group consisting of aqueous and alcoholic solutions and suspensions, oily solutions and suspensions and oil-in-water and water-in-oil emulsions.

43. The formulation of claim 36, which is a rectal formulation in the form of a suppository.

44. The formulation of claim 36, which is a transdermal formulation, wherein the carrier is selected from the group consisting of aqueous and alcoholic solutions, oily solutions and suspensions and oil-in-water and water-in-oil emulsions.

45. The formulation of claim 36, which is an iontophoretic transdermal formulation, wherein the carrier is selected from the group consisting of aqueous and alcoholic solutions, oily solutions and suspensions and oil-in-water and water-in-oil emulsions, and wherein the formulation further comprises a transdermal transport promoting agent.

46. An implantable capsule or cartridge, comprising the formulation of claim 44.

47. The formulation of claim 36, wherein the carrier is selected from the group consisting of aqueous and alcoholic solutions and suspensions, oily solutions and suspensions and oil-in-water and water-in-oil emulsions.

48. The formulation of claim 36, wherein the carrier comprises a hydrophobic carrier.

49. The formulation of claim 48, wherein the carrier comprises lipid vesicles or particles.

50. The formulation of claim 49, wherein the vesicles comprise liposomes, and the particles comprise microcrystals.

51. The formulation of claim 50, wherein the vesicles comprise liposomes which comprise the anti-sense oligonucleotide.

52. The formulation of claim 49, wherein the vesicles comprise N-(1-[2, 3-dioleoxyloxi] propyl) -N,N,N- trimethyl- ammonium methylsulfate.

53. The formulation of claim 36, comprising a respirable or inhalable formulation.

54. The formulation of claim 53, comprising an aerosol.

55. The formulation of claim 36, in single or multiple unit form.

56. The formulation of claim 36, in bulk.

57. An anti-bronchoconstriction, anti-allergy and anti-inflammatory kit, comprising

a delivery device;

in separate containers, a surfactant or mixtures of surfactants, and a nucleic acid comprising an oligonucleotide (oligo) effective to alleviate bronchoconstriction, allergy (ies) or inflammation, the oligo being selected from the group consisting of oligonucleotides which are anti-sense to target genes and mRNAs corresponding to the target genes, to genomic flanking regions selected from the group consisting of

intron and exon borders selected from the group consisting of the 5' end, the 3' end and the juxta-section between coding and non-coding regions, and to all segments of mRNA(s) encoding an adenosine A1, A2b and A3 receptors; anti-sense to target genes and mRNAs corresponding to the target genes, to genomic flanking regions selected from the group consisting of intron and exon borders selected from the group consisting of the 5' end, the 3' end and the juxta-section between coding and non-coding regions, and to all segments of mRNA(s) encoding an adenosine A1, A2b and A3 receptors, and consist of less than about 15% adenosine (A); combinations of the oligos; pharmaceutically acceptable salts of the oligos; and mixtures of the oligos, their combinations, their salts; and

instructions for its use;

and optionally an agent selected from the group consisting of other therapeutic and diagnostic agents, anti-oxidants, flavoring, fillers, volatile oils, dispersants, anti-oxidants, flavoring agents, propellants, preservatives, and buffering, RNA inactivating, cell-internalized or up-taken and coloring agents.

58. An anti-bronchoconstriction, anti-allergy and anti-inflammatory kit, comprising

a delivery device;

the composition of claim 1; and instructions for its use; and optionally

and optionally an agent selected from the group consisting of other therapeutic and diagnostic agents, anti-oxidants, flavoring, fillers, volatile oils, dispersants, anti-oxidants, flavoring agents, propellants, preservatives, and buffering, RNA inactivating, cell-internalized or up-taken and coloring agents.

59. The kit of claim 58, wherein the delivery device comprises a nebulizer which delivers single metered doses of the formulation.

60. The kit of claim 59, wherein

the nebulizer comprises an insufflator; and

the composition is provided in a piercable or openable capsule or cartridge.

61. The kit of claim 59, wherein

the delivery device comprises a pressurized inhaler; and

the composition comprises a suspension, solution or dry formulation of the agent.

62. The kit of claim 61, comprising a surfactant, a nucleic acid and a therapeutic agent selected from the group consisting of other anti-adenosine A_1, A_{2b} and A_3 receptor antagonists, adenosine A_{2a} receptor stimulants, anti-inflammatory agents, anti-histaminic agents, anti-allergic agents, anti-bacterial, anti-vials, analgesics, kidney activity maintenance and restoration agents, anti-cancer agents, adenosine, blood pressure controlling agents, and diuretics.

63. The kit of claim 61, wherein the solvent is selected from the group consisting of organic solvents and organic solvents mixed with one or more co-solvents.

64. The kit of claim 57, wherein the composition is provided in a capsule or cartridge.

65. An in vivo method of delivering a pharmaceutical composition to a target polynucleotide, comprising administering to a subject the composition of claim 1, comprising an amount of the surfactant and of the nucleic acid effective to reach the target polynucleotide.

66. The method of claim 65, wherein the disease or condition is associated with bronchoconstriction, allergy and/or inflammation of the lung.

67. The method of claim 66, wherein the disease or condition is selected from the group consisting of pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, Acute Respiratory Distress Syndrome (ARDS), renal damage or failure associated with ischemia and the administration of drugs and radioactive agents, side effects of adenosine and other anti-arrhythmic agents administered to treat arrhythmias and SupraVentricular Tachycardia (SVT) and to test cardiovascular function, ischemia, pain, cystic fibrosis,

pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD), and cancers selected from the group consisting of leukemias, lymphomas and carcinomas of the colon, breast, lung, pancreas, hepatocellular carcinoma, kidney, melanoma, hepatic, lung, breast and prostate, metastatic cancer, and those which are treated with radiation, chemotherapeutic, antibody therapy and phototherapeutic agents.

68. The method of claim 65, wherein the composition is administered into the subject's respiratory system.

69. The method of claim 65, wherein the agent is effective to reduce the production or availability or to increase the degradation of the adenosine receptor mRNA or to reduce the amount of the adenosine receptor.

70. The method of claim 65, wherein the agent is administered directly into the subject's lung (s).

71. The method of claim 65, wherein the agent is administered as a respirable aerosol.

72. The method of claim 65, wherein the disease or condition is associated with bronchoconstriction of the lung airways.

73. The method of claim 72, wherein the disease or condition is COPD, asthma, ARDS, side effects of adenosine administration or renal damage.

74. The method of claim 73, wherein the disease or condition is associated with inflammation.

75. The method of claim 74, wherein the therapeutic agent is selected from the group consisting of other adenosine A_1, A_{2b} and A_3 receptor inhibiting agents and adenosine A_{2a} receptor stimulating agents, anti-inflammatory agents, anti-bacterial agents, anti-sepsis agents, kidney activity maintenance and restoration agents and agents for the treatment of pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic

obstructive pulmonary disease (COPD), and cancers selected from the group consisting of leukemias, lymphomas and carcinomas of the colon, breast, lung, pancreas, hepatocellular carcinoma, kidney, melanoma, hepatic, lung, breast and prostate metastatic cancer, radiation agents, chemotherapeutic agents, antibody therapy agents, phototherapeutic agents, adenosine, and other anti-arrhythmic agents.

76. The method of claim 65, wherein the therapeutic agent is selected from the group consisting of anti-adenosine A_3 receptor agents.

77. The method of claim 65, wherein the disease or condition is associated with sepsis.

78. The method of claim 65, wherein the composition is administered by a topical or systemic route.

79. The method of claim 65, wherein the composition is administered orally, intracavitarily, intranasally, intraanally, intravaginally, intrauterally, intraarticularly, transdermally, intrabucally, intravenously, subcutaneously, intramuscularly, intravascularly, intratumorously, intraglandularly, intraocularly, intracranial, into an organ, intravascularly, intrathecally, intralymphatically, intraotically, by implantation, by inhalation, intradermally, intrapulmonarily, intraotically, by slow release, by sustained release and by a pump.

80. The method of claim 65, wherein the subject is a mammal.

81. The method of claim 80, wherein the mammals are selected from the group consisting of humans and animals.

82. The method of claim 81, wherein the mammal is a human.

83. The method of claim 81, wherein the subject is an animal.

84. The method of claim 65, wherein the anti-sense oligonucleotide is administered in amount of about 0.005 to about 150 mg/kg body weight.

85. The method of claim 84, wherein the anti-sense oligonucleotide is administered in an amount of about 0.01 to about 75 mg/kg body weight.

86. The method of claim 85, wherein the anti-sense oligonucleotide is

administered in an amount of about 1 to 50 mg/kg body weight.

87. The method of claim 65, which is a prophylactic method.

88. The method of claim 65, which is a therapeutic method.

89. The method of claim 65, wherein the oligo is obtained by

(a) selecting fragments of a target nucleic acid having at least 4 contiguous nucleic acids selected from the group consisting of G and C;

(b) obtaining a first oligonucleotide 4 to 60 nucleotide long which comprises the selected fragment and has a C and G nucleic acid content of up to and including about 15%; and

(c) obtaining a second oligonucleotide 4 to 60 nucleotide long comprising a sequence which is anti-sense to the selected fragment, the second oligonucleotide having an A base content of up to and including about 15%.

90. The method of claim 61, wherein the oligo consists of up to about 10% A.

91. The method of claim 90, wherein the oligo consists of up to about 5% A.

92. The method of claim 90, wherein the oligo consists of up to about 3% A.

93. The method of claim 93, wherein the oligo is A-free.

94. The method of claim 65, wherein the adenosine receptor target is selected from the group consisting of adenosine receptor genes and mRNAs and genomic flanking regions.

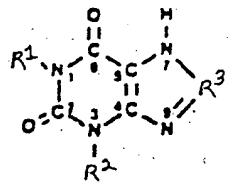
95. The method of claim 65, wherein at least one A is substituted by a universal base selected from the group consisting of heteroaromatic bases which bind to a thymidine base but have antagonist activity and less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, and heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

96. The method of claim 95, wherein all As are substituted by universal bases selected from the group consisting of heteroaromatic bases which bind to a thymidine base but have antagonist activity and less than about 0.3 of the adenosine base agonist activity at the adenosine A_1, A_{2b} and A_3 receptors, and heteroaromatic bases which have no activity or have an agonist activity at the adenosine A_{2a} receptor.

97. The method of claim 95, wherein the heteroaromatic bases are selected from the group consisting of pyrimidines and purines, which may be substituted by O, halo, NH_2, SH, SO, SO_2, SO_3, COOH and branched and fused primary and secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, which may be further substituted by O, halo, NH_2, primary, secondary and tertiary amine, SH, SO, SO_2, SO_3, cycloalkyl, heterocycloalkyl and heteroaryl.

98. The method of claim 97, wherein the pyrimidines and purines are substituted at positions 1, 2, 3, 4, 7 and 8.

99. The method of claim 98, wherein the pyrimidines and purines are selected from the group consisting of theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline and xantine having the chemical formula



wherein R^1 and R^2 are independently H, alkyl, alkenyl or alkynyl and R^3 is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH_2-alkylamino-ketoxyalkyloxy-aryl and mono and dialkylaminoalkyl-N-alkylamino-SO_2 aryl.

100. The method of claim 99, wherein the universal base is selected from the group consisting of 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-

deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methoxyaminopurine.

101. The method of claim 65, further comprising methylating at least one cytosine (mC) if a CpG dinucleotide if present in the oligo(s).

102. The method of claim 65, further comprising substituting at least one mononucleotide linking phosphodiester residue of the anti-sense oligonucleotide(s) with a residue selected from the group consisting of methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methyimino), methyleneoxy (methylimino), 2'-O-methyl, phosphoramidate residues, and combinations thereof.

103. The method of claim 102, wherein all phosphodiester residues are substituted.

104. The method of claim 65, further comprising linking the anti-sense oligonucleotide to an agent selected from the group consisting of cell internalized and up-taken agent(s) and cell targeting agents.

105. The method of claim 104, wherein the cell internalized or up taken agent is selected from the group consisting of transferrin, asialoglycoprotein, and streptavidin.

106. The method of claim 104, wherein the cell targeting agent is a vector.

107. The method of claim 106, wherein the vector to which the agent is operatively linked is a prokaryotic or eukaryotic vector.